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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
CHERNYSHEV,O	

ART UNIT	PAPER NUMBER
1646	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/624,965	Applicant(s) MASTERS ET AL.	
	Examiner Olga N. Chernyshev	Art Unit 1646	

-- Th MAILING DATE of this communication appears on the cov r sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 27-33 is/are pending in the application.

4a) Of the above claim(s) 27 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 28-33 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8, ___ .
18)☒ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

Response to Amendment

1. Claims 15-21, 25 and 26 have been cancelled, claims 28-33 have been added as requested in the Amendment of paper #7, filed on April 19, 2001. Claims 27-33 are pending in the instant application.

Election/Restrictions

2. Applicant's election with traverse of Group I in Paper No. 5 is acknowledged. The traversal is on the ground(s) that the inventions of Groups I and II are related. This is not found persuasive because an application may properly be required to be restricted to one of two or more claimed inventions if they are able to support separate patents and they are either independent (MPEP § 806.04 - § 806.04 (j)) or distinct (MPEP § 806.05 - § 806.05 (i)). The Examiner has shown that the Groups are independent or distinct for the reasons in the previous Office action (see Paper #3). Furthermore, MPEP § 803 provides that the separate classification (i.e., class and subclass) of distinct inventions is sufficient to establish a *prima facie* case that the search and examination of the plural inventions would impose a serious burden upon the Examiner; such separate classification was set forth in the Office action mailed 05 January, 2001 (Paper #3) Applicant has offered no evidence to rebut this showing. Therefore, a *prima facie* case for a serious search burden was presented in Paper #3 and Applicant has offered no evidence to rebut this showing.

The requirement is still deemed proper and is therefore made FINAL.

Claim 27 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 5.

Claims 28-33 are under examination in the instant office action.

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Specification

4. The disclosure is objected to because of the following informalities: on page 2, line 8 ".at" should be "that", perhaps. Page 7, line 11 "ATP" should be "APP", perhaps. Page 7, line 27 "zinc effects" should be "zinc affects", perhaps. Page 10, lines 7-9, sentence "Using such agents..." needs clarification for it is not clear what are the compartments of Alzheimer's disease referred to. Page 32, Example 6: The very last sentence does not make sense. Clarification is required.

Appropriate corrections are required.

5. Applicant is reminded of the proper content of the specification.

Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a). The title of the invention should be placed at the top of the first page of the specification. It should be brief but technically accurate and descriptive, preferably from two to seven words.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) Reference to a "Microfiche Appendix": See 37CFR 1.96(c) and MPEP § 608.05. The total number of microfiche and the total number frames should be specified.

(e) Background of the Invention: The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(f) Brief Summary of the Invention: A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(g) **Brief Description of the Several Views of the Drawing(s): A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.**

(h) Detailed Description of the Invention: A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. This item may also be titled "Best Mode for Carrying Out the Invention." Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another

patent or readily available publication which adequately describes the subject matter.

(i) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet. (37 CFR 1.52(b)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps.

(j) Abstract of the Disclosure: A brief narrative of the disclosure as a whole in a single paragraph of 250 words or less on a separate sheet following the claims.

(k) Drawings: See 37 CFR 1.81, 1.83-1.85, and MPEP § 608.02.

(l) Sequence Listing: See 37 CFR 1.821-1.825.

Part (g) is highlighted by the Examiner. Appropriate correction regarding Brief description of the drawings is required.

6. The specification contains list of references on pages 36-38. However, there is little referral to the references in the text of the specification. It is suggested that references be included in the text of the specification. If Applicant adopts this suggestion a substitute specification will be required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 28-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method for treating Alzheimer's disease in a patient by means of modulating divalent or trivalent cation and /or heparin with amyloid precursor protein (APP). The specification describes theoretical basis for such a treatment. However, the given description is found to be controversial, confusing and not supported by experimental data, which makes certain statements lacking scientific credibility. For example, on page 1 of the instant specification it reads that "At least one form of APP has been shown to have neurotrophic activity, i.e. capable of promoting the survival or outgrowth of nerve processes" (lines 28-29). This fact is very well known in the art and it is recognized that a normal function of APP is indeed being a neurotrophic factor, among others. That's is why it is controversial to conclude that elevation of APP mRNA in Alzheimer's patients, Down's Syndrome patients or in experimental models with zinc loading will lead to the abnormal cleavage of APP and future amyloid depositions (page 6, lines 21-30). The initial elevation of APP mRNA might just as well be a part of a normal response to an oxidative stress, for example (in case of Alzheimer's disease or Down's Syndrome) or elevated concentration of zinc (in case of experiments with zinc loading, page 6, lines 25-27) and in fact may be the beginning of a process of damage repair, which is a normal function of APP. Nevertheless, according to Applicants "This provides a basis for therapeutic intervention based on modulating divalent cation interaction with APP" (page 6, lines 28-31).

The specification also discloses heparin function, which is, again, not supported by any references to any scientific publication (page 7, lines 21-27). Explanation of involvement of zinc

and zinc binding agents and their interaction with heparin and APP is very confusing (for example, page 7, line 29, "low zinc concentrations (above about 1 μm)- emphasis added by the Examiner) and, again, is not supported by any data or references.

Besides presenting a theoretical basis for the claimed invention, the instant specification does not provide any guidance on how to treat Alzheimer's disease by method of using an agent that modulates the interaction between divalent or trivalent cation and/ or heparin with APP, thus leaving a skilled artisan to perform an undue experimentation in order to practice the full scope of the invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

The state of the art of treating Alzheimer's disease is very unpredictable. The causes and etiology of the disease are not fully discovered yet, absent evidence to the contrary. The instant specification does not teach how to treat Alzheimer's disease. Nor it is disclosed how "a therapeutically effective amount of an agent" can effectively treat any or all of the symptoms of Alzheimer's disease. It is unknown, and Applicants provide no guidance as to what symptoms of Alzheimer's disease are corrected by "an agent".

In view of the lack of teachings and unpredictability of the art set forth earlier, and also the total absence of the working examples, the instant specification is not found to be enabling

for a method for treating Alzheimer's disease. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use Applicants' invention as currently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 28-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 28 is indefinite because it is not clear from the claim or the specification what "a therapeutically effective amount of an agent" is. No such "effective amount" is indicated, therefore the metes and bounds of such cannot be determined.

Finally, it is not clear what is meant by "interaction" within CNS. Clarification is required.

10. Claim 31 is an improper Markush claim (see MPEP 2173.05(h)). The claim recites "selected for sodium citrate etc." which is improper Markush language. One acceptable form of alternative expression, which is commonly referred to as a Markush group, recites members as being "selected from the group consisting of A, B, and C". See *Ex parte Markush*, 1925 C.D. 126 (Comm'r Pat. 1925). Alternatively, the claim could recite eliminate the phrase "selected from the group consisting of" and retain the "or".

11. Claims 29-30 and 32-33 are indefinite for being dependent from the indefinite claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 28-31 and 33 rejected under 35 U.S.C. 102(b) as being anticipated by Cardelli et al (J Am Geriatr Soc, 1985, 33, 548-560).

Cardelli et al teach the treatment of two individuals being diagnosed with Alzheimer's disease with ETDA (Case 1 and Case 2, pages 548-549). This anticipates limitations of claims 28-31 and 33.

Conclusion

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-0294 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D. *OC*
June 7, 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud